

Fig. 1

Human A4 Receptor

1	TTGAGCCGGCAGACTCGGAAAAGTAGCTGGAGCCGGAGCAGGACAGAACCTGTGTGCTGCAGACGGGCTTGGTGGATTCTGTGGTTCCCTGCCGCCGACAGGGCTCGCCGGGAGAGGTTTCATC	120
121	ATGAATGAGAAATGGGACACAAAACCTCTTCAGAAAACCTGGCATCCCATCTGGAATGTCAAATGACACAAAAGCATCATCTGTACTCAGATATTAATAATTACCTATATGTGAACCTACTATCTTCAC	240
1	M N E K W D T N S S E N W H P I W N V N D T K H L Y S D I N I T Y V N Y Y L H	40
241	CAGCCTCAAGTGGCAGCAATCTTCATTAATTTCCCTACTTTTCTGATCTTTCTTCTGATCTTTCTTTTGTGCATGATGGGAAATACTGTGGTTTGTCTTTATTTGTAATGAGGAACAACAAATATGCACACAGTCACT	360
41	Q P Q V A A I F I I S Y F L I F F L C M M G N T V V C F I V M R N K H M H T V T	80
361	AATCTCTTCATCTTAAACCTGGCCATAAGTGATTTACTAGTTGGCATATTTCTGCATGCCCTATAACACTGCTGGACAAATATTATAGCAGGATGGCCATTTTGGAAACACGATGTGCAAGATC	480
81	N L F I L N L A I S D L L V G I F C M P I T L L D N I I A G W P F G N T M C K I	120
481	AGTGGATTGGTCCAGGGAATATCTGTGCGCAGCTTCAGTCTTTACGTTAGTTGCAATTGCTGTAGATAGGTTCCAGTGTGTGGTCTACCCCTTTTAAACCAAAGCTCACCTATCAAGACAGCG	600
121	S G L V Q G I S V A A S V F T L V A I A V D R F Q C V Y P F K P K L T I K T A	160
601	TTTGTCAATTATATGATCATCTGGGTCTTAGCCATCACCATTTATGTCTCCATCTGCAGTAATGTTACATGTGCCAAGAAAGAAAATATTACCGAGTGAAGTCAACTCCAGAAATAAAACC	720
161	F V I I M I I W V L A I T I M S P S A V M L H V Q E E K Y Y R V R L N S Q N K T	200
721	AGTCCAGTCTACTGGTGGCGGAAGACTGGCCAAATCAGGAAGATCTACACCACCTGTGCTGTTTGCCAAACATCTACCTGGCTCCCTCTCCCTCATTTGTTCATCATGTATGGA	840
201	S P V Y W C R E D W P N Q E M R K I Y T T V L F A N I Y L A P L S L I V I M Y G	240
841	AGGATTGGAATTTCACTCTTCAGGGCTGCAGTTCCTCACACAGGCAGGAAGAACCCAGGAGCAGTGGCACCTGGTGTCCAGGAAGAACGAGAAGATCATTTAAGATGCTCCTGTATGTGGCC	960
241	R I G I S L F R A A V P H T G R K N Q E Q W H V V S R K K Q K I I K M L L I V A	280
961	CTGCTTTTATTTCTCTCATGGCTGCCCTGTGGACTCTAATGATGCTCTCAGACTACGCTGACCCTTTCTCCAAATGAACCTGCAGATCATCAACATCTACATCTACCCCTTTTGCACACTGG	1080
281	L L F I L S W L P L W T L M L S D Y A D L S P N E L Q I I N I Y I Y P F A H W	320
1081	CTGGCATTCGGCAACAGCAGTGTCAATCCCATCATTTTATGGTTTCTTCAACGAGAAATTTCCGCCGTGGTTTCCAGACTCCAGCTTTCCAGCTCCAGCTCTGCCAAAAGAGCAAGCAAGCCCTATG	1200
321	L A F G N S S V N P I I Y G F F N E N F R R G F Q E A F Q L Q L C Q K R A K P M	360
1201	GAAGCTTATACCCCTAAAGCTAAAGCCATGTGCTCATAAACACATCTAATCAGCTTGTCCAGGAATCTACATTTCAAACCCCTCATGGGGAAACCTTGTCTTTATAGGAAAAGTGTGAA	1320
361	E A Y T L K A K S H V L I N T S N Q L V Q E S T F Q N P H G E T L L Y R K S A E	400
1321	AAACCCCAACAGGAATTAGTGGAAGAATTAAAGAAACTACTAACACGAGTGAGATTTAAAGAGAGCTAGTGTGATAATCCTAACTCTACTACGCAATTATATATTAAATCCATTGC	1440
401	K P Q Q Q E L V M E L K E T T N S S E I *	421

TM1	TM2	TM3	TM4	TM5	TM6	TM7
47-69	82-104	121-141	160-182	218-240	275-297	312-336

Fig. 2

Amino Acid Homologies of A4 and Related Mammalian Receptors

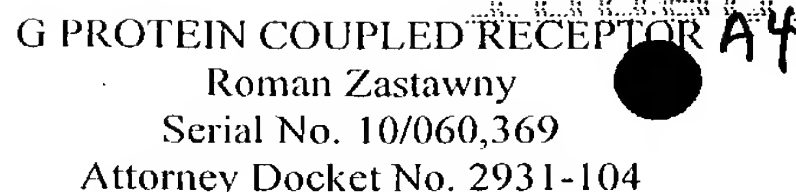
Note: All sequences are human
Numbers below represent % similarity / % identity

A4	Orexin1	Orexin2	Y1	Y2	Y4	Y5	Gastrin	CCKA	NK1	Mu
100	59/32	61/32	63/31	61/30	59/28	61/28	61/28	63/31	55/26	62/25
	100	84/69	58/26	59/32	64/32	61/26	58/27	59/30	59/32	58/26
		100	60/27	60/31	63/32	59/26	61/29	58/29	56/31	58/28
			100	63/31	71/43	66/32	60/30	56/28	54/29	54/24
				100	62/33	63/32	56/27	56/29	59/30	57/24
					100	64/29	54/29	56/28	53/26	54/25
						100	58/28	55/26	57/24	61/26
							100	73/50	55/27	58/24
								100	57/30	55/26
									100	60/26
										100

Legend: GenBank Accession No Description

Legend:
Code:

Orexin1	AF041243	Human Orexin receptor-1
Orexin2	AF041245	Human Orexin receptor-2
Y1	P25929	Human Neuropeptide receptor Type1
Y2	P49146	Human Neuropeptide receptor Type2
Y4	P50391	Human Neuropeptide receptor Type4
Y5	U56079	Human Neuropeptide receptor Type5
Gastrin	P32239	Human Gastrin/Cholecystokinin Type B receptor
CCKA	P32238	Human Cholecystokinin Type A receptor
NK1	P25103	Human Neurokinin-1/Substance-P receptor
Mu	P35372	Human Mu-type opioid receptor

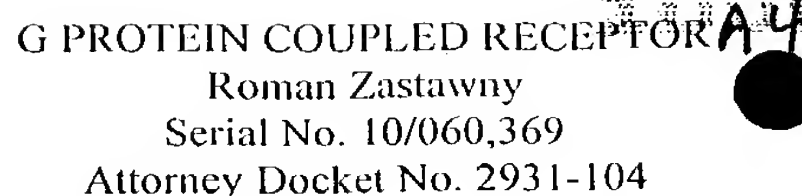


A4 vs. Human Y1 receptor

Percent Similarity: 63.032

Percent Identity: 30.585

1	MNEKWDTNSSSENWHPIWNV.NDTKHHLYSDINXTYVNYYLHQPPQVAAIFI	49
1MNSTLFSQVENHSVHSNFSEKNAQLLAFENDDCHLPLAMI	40
50	ISXFL....IFFLCMMGNTVVCFIVMRNKHMHMTVTNLFILNLAISDLLVG	95
41	FTLALAYGAVIILGVSGNLALIIIIILKQKEMRNVNLTNLIIVNLSFSDLLVA	90
96	IFCMPITLLDNIIAGWPFGNTMCKISGLVQGISVAASVFTLVAVIAVDRFQ	145
91	IMCLPFTFVYTLMDHWVFGAMCKLNPFVQCVSITVSIFSLVLI AVERHQ	140
146	CVVYPFKPKLTIKTAFVIIMLIWVLAITIMSPSAVMLHVQEEKYYRVRLN	195
141	LIINPRGWRPNNRHAYVGIAVIWVLAVASSLPFLIYQVMTDEPFQNVTL	190
196	SQNKTSPVYWCREDPNQEMRKIYTTVLFANIYLAFLSLIVIMYGRIGIS	245
191	AYKDK...YVCFDQFSDSHRLSYTTLLLVLYQYFGPLCFIFICYFKIYIR	237
246	LFRAAVPHTGRKNQEQWHVVSRRKKQKIIKMLLIVALLFILSWLPLWTLMM	295
238	LKRRNNMMDKMRDNKYR...SSETKRINIMLLSIVVAFAVCWLPLTIFNT	284
296	LSDYADLSPNELQIINIY....IYPFAHWLAFGNSSVNPIIYGFFNENFR	341
285	VFDWNH.....QIIATCNHNLFLCHLTAMISTCVNPIFYGFLNKNFQ	328
342	RGFQEAFLQLCQKRAKPMAYTLKAKSHVLINTSNQLVQESTFQNPHE	391
329	RDLQ..FFNFCDFRSRD.DDYETIAMSTMHTDVSKTSLK.....QAS	368
392	TLLYRKSAEKPQQELVMEELKETNSSEI*	421
369	PVAFKKINNNDNEKI*.....	385



SECRET

1	MSGTKLEDSPPCRNWSSASELNETQEPFLNPTDYDDEEFLRYLWREYLHP	50
1	MNEKW..DTNSSENWHPIWNVNDTKHHLYS DINTYVNY.....YLHQ	41
51	KEYEVLIAGYIIVFVVALIGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD	100
42	PQVAAIFIISXFLIFFLCMMGNTVVC FIVMRNKHMHMTVTNLFILNLAISD	91
101	VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL	150
92	LLVGIFCMPITLLDNIIAGWPFGNTMCKISGLVQGISVAASVFTLVIAIAV	141
151	DRWYAICHPLMFKSTAKRARN SIVIIWIVSCIIMIPQAIVME.....CST	195
142	DRFQCVVYPFKPKLTIKTA FVIIMI IWVLAITIMSPSAVMLHVQEKEYR	191
196	VFPGLANKTTLFTVCDERWGGEIYPKMYHICFFLVTYMAPLCLMVLAYLQ	245
192	VRLNSQNKTS PVYWCREDWPNQEMRKIYTTVLFANIY LAPLSLIVIMYGR	241
246	IFRKLWCRQIPGTSSVVQRKWKPLQPV SQPRGPGQPTKSRMSAVAAEIKQ	295
242	IGISLFRAAVPHTGEKNQE QWHVV.....	265
296	IRARRKTARMLMVLLVFAICYLPISILNV LKRVFGMFAHTEDRET VYAW	345
266	SRKKQKIIKMLLIVALLFILSWLPLW TLMMLSDYADLSPNELQIINIYI.	314
346	FTFSHWLVYANSAANPIIYNFLSGKFREEFKAAFSCCCLGVHHRQEDRLT	395
315	YPFAHWLAFGNSSVNPIIYGFFNENFR RGFQEAFQ...LQLCQKRAKPME	361
396	RGRTSTESRKSLTT.....QISNFDN.....ISKLSEQVVLTSI	429
362	AYTLKAKSHVLINTSNQLVQESTFQ NPHGETLLYRKSAEKPQQELVMEEL	411
430	STLPAANGAGPLQNW*	445
412	KETTSSEI*.....	421



A4 vs. Human CCK receptor

Fig.5

Percent Similarity: 63.514

Percent Identity: 31.081

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1  ..MNEKWDTNSSSENWHPiWNVNDTKHHLYSDINXTYVNYYLHQPV.... 44
   : : : .|:|          | |.. : : | |. :|:| |:..
1 MDVVDSLLVNGS.....NITPPCELGLENETL..FCLDQPRPSKEW 39

45  .AAIFIISXFLIFFLCMMGNTVVCfIVMRNKHMHtVTNLFILNLAIStLL 93
   :|: |: |||:|:|:| |:|.. : :| |:|:| |:| |:| |:| |:| |:| |:| |:|
40 QPAVQILLYSLIFLLSVLGNTLVITVLIRNKRMRtVTNIFLLSLAVSDLM 89

94  VGIFCmPITLLDNIIAGWPFGNTMCKISGLVQGISVAASVFTLVAIaVDR 143
   : :| |:| |:| |:| : : | |:| |:| |:| |:| |:| |:| |:| |:| |:|
90 LCLFCmPFNLIPNLLKDFIFGSaVCKTtTYFMGTSVSVStFNLVAISLER 139

144 FQCVVYPFKPKL..TIKtAFVIIMIiWVLAItIMSPSAVMLHVQEEKYR 191
   : : : : | : : : | . | : : | . | : : | | | . | : : : :
140 YGAICKPLQSRVWQTKSHALKVIAATWCLStFTIMTPYPIYSNL..... 182

192 VRLNSQNKtSPVYWCREdWPNQEMRKIYtTVLFANIYLAPLSLIVIMYGR 241
   | : : : |:| : : || :| |:| : : | . |:| : : | | : : : | |
183 VPFTKNNNQTA.NMCRFLLPNDVMQqSWHTFLLLILFLIPGIVMMVAYGL 231

242 IGISLFRA....AVPHTGRKNQEQWHVVSrk..... 268
   |:| |:| : : | : : : |:| : : | |
232 ISLELYQGIKFEASQKKSakerKPStTSSGKYEDSDGCYLQKTRPPRKLE 281

269 .....KQKIiKMLLiVALLFiLSWLPLWT 292
   | : : |:| |:| : : : |:| |:| |:| |:| : :
282 LRQLSTGSSSRANRIRSNSSaANLMAKKRVIRMLIVIVVLFFLCWMPiFS 331

293 LMMLSDYADLSPNELQIINIYIYPFAHWLAFGNSSVNPIIYGFFNENFRR 342
   : : | : | : : : : | :| : : : : |:| |:| |:| |:| |:| |:|
332 ANAWRAYDTASAE..RRLSGTPISFiLLSYtSScVNPIIYCFMNRfRL 379

343 GFQEAfQLQLCQKRAKPMaYTLKAKSHVLINTSNQLVQEstFQNPHGt 392
   || : : | : : : : : : : : : : : : | : : :
380 GFMATF.....PCCPNPGPPGARGEVGEEEEGGTTGASLSRF 416

393 LLYRKSAEKpQqELVMEELKETTNSSEI* 421
   . : . | | . | . |
417 SYSHMSASVPPQ..... 428
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Fig.6

